Poster Presentation

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Structural characterization of Asparagine Synthase A from Trypanosoma cruzi

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In the Americas, 7.6 million people are infected with Trypanosoma cruzi, causative agent of Chagas disease. Although the parasite life cycle was determined in 1909, the drugs developed to eliminate T. cruzi have low efficacy and high toxicity, especially when the disease is in the chronic phase. Extracellular proteins secreted by protozoan parasites are key mediators in host-parasite interactions. Proteomic approaches have been used to investigate protein secreted by parasites intra-and extra-cellular and these studies led to the identification of a large number of proteins directly involved in fundamental processes of host-parasite interactions. There is evidence that the enzyme Asparagine synthase A from Trypanosoma cruzi is secreted during parasite invasion. This enzyme produces asparagine, glutamate, AMP and pyrophosphate in the presence of aspartate, ATP and glutamine or NH3. Although asparagine is of vital importance for the correct synthesis of proteins and post-translational modifications such as N-glycosylation, there is no structural characterization of this enzyme. In this work, the protein asparagine synthase A of T. cruzi was recombinantly-produced and purified. Its biochemical characterization shows the optimum activity at pH 7.5 with preference for NH3 than glutamate. SAXS and DLS indicate changes in quaternary structure dependent on pH. Those modifications influence enzyme activity and its thermal stability. Structural analysis indicates the determinants of preference for NH3 and indicate potential sites of inhibition of this protein.

Keywords: Asparagine Synthase A, Oligomerization, Neglected diseases